Venous outflow and inflow resistance in health and venous disease

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Purpose: The purpose of this study was to develop a physiologic method to measure outflow and inflow from the lower extremities and thus to quantify the degree of venous valvular insufficiency and venous obstructive disease.
Methods: Calibrated photoplethysmography was used in combination with passive changes in hydrostatic pressure, by leg elevation followed by repositioning of the leg to the original sitting position. With the principle of venous occlusion plethysmography, timed volume changes were then used to calculate the outflow and inflow. The inflow and outflow units were the percentage of optical reflectance (%OR) per minute. The respective resistances were calculated by identifying the hydrostatic pressure distance from the third intercostal space to the probe site that is inducing these site changes. The resistance units were millimeters of Mercury × minutes per %OR.
Results: Four groups of subjects were examined: normal individuals, patients with venous valvular insufficiency, deep venous thrombosis, and a combination of both. The most significant differences in outflow values were found between the control group (81.77% OR/min) and the deep venous thrombosis group (28.47% OR/min). In contrast, the most significant differences in inflow values were found between the control group (9.67% OR/min) and the venous valvular insufficiency group (108.61% OR/min). The resistances changed correspondingly.
Conclusion: The application of calibrated photoplethysmography in conjunction with induced changes in leg hydrostatic pressure proved to be an effective physiologic method to noninvasively quantify venous hemodynamics in normal control subjects, patients with venous valvular insufficiency, venous obstructive disease, or both. (J Vasc Surg 2000;31:472-6.)

Before the advent of duplex ultrasonography, photoplethysmography was frequently used to diagnose venous valvular insufficiency (VVI) on the basis of the refilling time after standardized exercise (eg, dorsiflexion).[1,2] An improved photoplethysmography system known as light reflexion rheography[3] increased its acceptance, especially in Europe, because of its high degree of user friendliness. A number of investigators found the refilling time, which is the only quantitative parameter obtainable with standard photoplethysmography, to have a reasonable accuracy to detect VVI.[4-12] Some authors, however, found the current method still wanting because of the limited quantitative information obtained[13-16] and because possible venous obstructive disease cannot be diagnosed.

We decided to develop a photoplethysmography system that can be calibrated photoplethysmography (C-PPG) and that permits quantification of blood volume displacements that are induced by changes in leg position, affecting the leg hydrostatic pressure.

METHOD

Principle of C-PPG. Quantification of photoplethysmographic responses was achieved by a defined increase or decrease in light intensity of the light-emitting diode incorporated in the photoplethysmography probe.[17] Fig 1 describes the simple diagram that consists of an adjustable resistor and an additional fixed resistor. The adjustable resistor is adjusted so that, by short-circuiting it, the current (and the light intensity) will increase by 5%, as monitored across the fixed resistance. This calibration unit is connected between a standard photoplethys-

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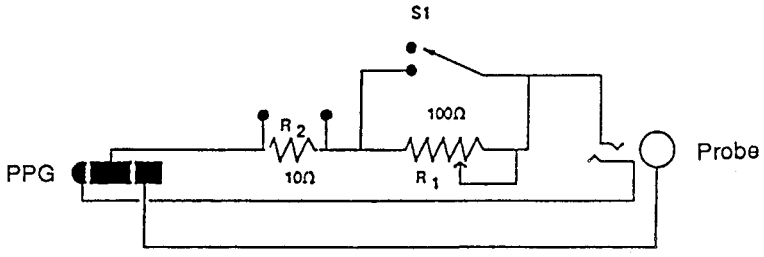

Fig 1. Diagram of the calibration unit connected between the photoplethysmography (*PPG*) instrument and the probe. R_1, Adjustable calibration resistance; R_2, fixed resistance across which the change in voltage drop is monitored; *S1*, short-circuiting switch.

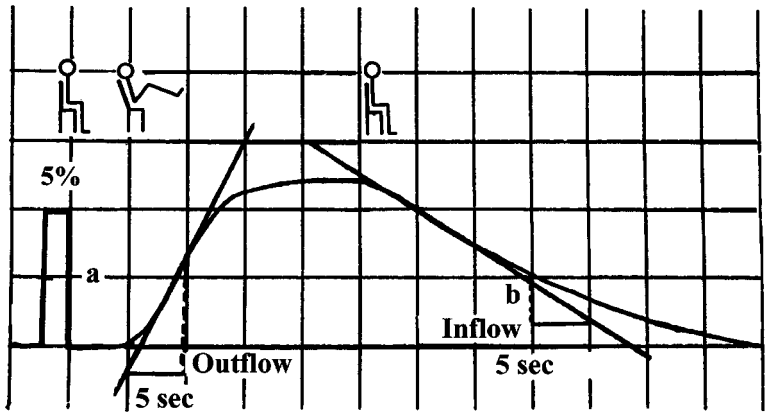

Fig 2. C-PPG tracing. *a*, Calibration deflection; *b*, volume change in 5 seconds.

mography instrument and the probe. Our results were obtained by using a Nicolet-IMEX Plethysmograph 3000 (Nicolet-IMEX, Golden, Colo) with a built-in calibration system.

Description of the test. The subject sits in a comfortable reclining armchair, and a photoplethysmographic probe is taped to the skin about 8 cm above the medial malleolus. After a steady state is reached, a calibration is performed (changing the light intensity of the probe light-emitting diode by 5%; Fig 2). The subject's legs are then elevated quickly above heart level; after a new steady state is reached, the legs are lowered as fast as possible. The subject's participation must be completely passive to prevent muscle contraction artifacts.

Evaluation of the tracing. In inverse analogy to well-known venous occlusion plethysmography, in which a sudden increase in cuff pressure stops the venous outflow, here a sudden decrease in hydrostatic pressure (leg elevation) induces an "outflow" of blood from the examined leg. Similarly, by repositioning the leg (sudden increase in hydrostatic pressure), "inflow" is recorded.

Assuming the 5% calibration deflection (*a*) and the volume change in 5 seconds (*b*), a simple ratio is used:

$$a: 5\% = b: x$$

$$x = \frac{5\% \times b}{a}$$

Flow (percent of optical reflectance [%OR] / min) $- 12 \times$

(Note: the multiplier 12 is used to express the flow rate per minute if *b* is read off after 5 seconds.)

The units are %OR / min.

The distance from the third intercostal space to the probe site was measured to determine the decrease in hydrostatic pressure induced by the leg elevation (from the dependent position to heart level). Conversely, the same hydrostatic pressure (but in the opposite direction) was responsible for the inflow when the leg was returned to the depen-

Table I. Summary of inflow and outflow data

	Outflow (%OR/min)	*Outflow resistance (mm Hg × min/%OR)*	*Inflow (%OR/min)*	*Inflow resistance (mm Hg × min/%OR)*
Normal	90.30 ± 11.38	0.8268 ± 0.10	9.67 ± 1.18	7.707 ± 0.887
VVI	84.52 ± 7.14	1.0461 ± 0.12	108.61 ± 13.97	1.084 ± 0.168
DVT	28.47 ± 1.66	2.4760 ± 0.143	21.09 ± 4.20	6.202 ± 0.547
DVT + VVI	37.82 ± 3.23	2.6333 ± 0.344	77.8 ± 6.35	1.136 ± 0.113

Table II. Reproducibility-expressed by the coefficient of variation

	Coefficient of variation (%)
Outflow	11.83 ± 3.35
Outflow resistance	12.52 ± 3.81
Inflow	14.23 ± 6.36
Inflow resistance	14.54 ± 6.69

dent position. The results were converted to millimeters of Mercury by multiplying the distance in centimeters by 0.74. The outflow and inflow resistance was then calculated by dividing the hydrostatic pressure by the outflow and inflow, respectively. The resistance units are mm Hg × min/%OR. The calculations were performed blinded to the results of the duplex scanning results.

Control subjects and patients. Twenty-four control subjects (1 leg per subject) served as a comparison to 31 patients with VVI (21 legs), venous obstructive disease (5 legs), and both pathologies (15 legs).

All patients underwent an examination by duplex ultrasonography (Diasonics VST; Santa Clara, Calif). Standard examination procedure was used to search for VVI (reversed Trendelenburg position, manual proximal compression, reflux > 0.5 sec)[18]; compressibility and echogenicity were criteria to establish the diagnosis of venous obstructive disease.[19] This group included patients with partial and complete obstructions. Only patients with chronic venous obstructive disease of the deep venous system were included in this study. The study was approved by the UCSD Human Subjects Program Review Board.

Results are presented as mean values with SEM. Statistical significance of differences between four different groups was determined on the basis of a probability value less than .05.

RESULTS

Normal control subjects. Studies were performed on 24 legs of control subjects with no history of venous disease. The mean outflow value was 81.77 ± 5.98 %OR/min, with the outflow resistance at 0.913 mm Hg × min/%OR ± 0.11. The inflow rate was almost 10 times smaller, at 9.67 ± 1.18 %OR/min, with the inflow resistance accordingly higher at 7.71 mm Hg × min/%OR ± 0.89 (Table I).

Reproducibility was determined on nine normal control subjects by measurements performed in 3 consecutive days at approximately the same time of the day (between 10 and 12 AM). The results are summarized in Table II. The coefficient of variation varied from 11.44% to 9.44%.

VVI. Altogether 13 patients (21 legs) were classified in this category. The outflow rate was nearly the same as in the control group: 84.52 ± 7.14 %OR/min, with an outflow resistance of 1.046 mm Hg × min/%OR ± 0.11 (Table I). The inflow rate, however, was about 11 times higher than in the normal control group: 108.6 ± 13.97 %OR/min, with a correspondingly reduced inflow resistance of 1.08 mm Hg × min/%OR ± 0.17.

Deep venous thrombosis. Five patients with a diagnosis of deep venous thrombosis (DVT; 5 legs) were included in this group. Outflow was significantly reduced, compared with the control subjects and the VVI group: 28.47 ± 1.66 %OR/min, with an obviously increased outflow resistance of 2.48 mm Hg × min/%OR ± 0.143 (Table I). Inflow and inflow resistance values were close to those of the normal control group: 21.09 ± 4.20 %OR/min and 6.20 mm Hg × min/%OR ± 0.55, respectively.

DVT with VVI (DVT + VVI). This group (13 patients; 15 legs) yielded values pathognomonic for both hemodynamic derangements: decreased outflow and increased inflow. The mean outflow value of 37.82 ± 3.23 %OR/min, which was significantly lower than in the control group (81.77 %OR/min), although the inflow of 77.80 ± 6.35 %OR/min was approximately eight times higher than that obtained

Table III. Statistical summary

	Outflow		*Inflow*		*Outflow resistance*		*Inflow resistance*	
	t	*P*	*t*	*P*	*t*	*P*	*t*	*P*
Control vs VVI	0.05	NS	6.22	<.0001	0.25	NS	6.33	<.0001
Control vs DVT	4.82	<.0007	0.26	NS	10.74	<.0001	0.96	NS
Control vs DVT + VVI	3.88	<.0005	10.81	<.0001	2.87	<.005	6.24	<.0001
VVI vs DVT	1.02	NS	5.88	<.0001	7.18	<.0001	9.14	<.0001
VVI vs (DVT + VVI)	0.74	NS	1.13	NS	2.69	<.005	0.61	NS
DVT vs (DVT + VVI)	0.72	NS	9.03	<.0001	1.05	NS	9.16	<.0001

in the control group (9.67 %OR / min). The outflow and inflow resistances were correspondingly abnormal. Table I summarizes these results, including the mean values and SEM.

As presented in Table III, the most significant outflow differences were found between the control and DVT group, although inflow differences were not significant.

DISCUSSION

The application of C-PPG permits a quantitative evaluation of hemodynamic changes induced by changes in leg position. The timed volume changes, outflow with leg elevation and inflow with returning to the original leg (sitting) position, make it possible to calculate flow rate–related values, with the use of the principle of venous occlusion plethysmography. The results are expressed in percentage of optical reflectance (%OR / min) based on the calibrated change in the source of light intensity.[17]

The hydrostatic pressure is determined by measuring the probe-heart distance (third intercostal space), and therefore the corresponding resistance can be calculated (mm Hg × min / %OR).

There are some technical difficulties to be avoided. The change in leg position should be achieved completely passively (ie, subject's leg should be lifted by the heel) to minimize artifacts. Compression of the malleolar region can also induce an artifact. The artifact-free leg position change is best achieved when the subject is sitting in a reclining chair so that the subject can recline as much as necessary and the hip joint movement is not exaggerated.

The most significant differences in inflow were between the control group and patients with VVI. Similarly, a highly significant difference in outflow value was found between the control group and patients with DVT (Tables I and III). As expected, both parameters were found to be significantly different from the control group in the group of patients with DVT combined with VVI.

Photoplethysmography has an intrinsic advantage because the optimal photoplethysmographic changes are obtained from the medial aspect of the malleolus, an area critical for the development of trophic changes induced by venous hypertension.

With standard photoplethysmography instrumentation, the recovery time is the only quantitative parameter that is affected by VVI. C-PPG offers, in addition to recovery time, a quantifiable measure of local blood volume displacement induced either by exercise[17] or by leg elevation, thus permitting the calculation of outflow and inflow as described.

The use of the subject's hydrostatic pressure, which enables the calculation of outflow and inflow resistance, introduces a factor specific to the subject's height.

It can be argued that duplex ultrasonography is now considered the diagnostic gold standard. Aside from the much higher cost and the longer examination time, this method is sometimes less than optimal in answering questions of venous obstructive disease of the calf, especially when functional testing is considered. We feel that C-PPG is highly useful as a fast physiologic screening method, especially in outpatient clinic conditions.

Future studies that examine a larger number of patients especially with venous obstructive disease, with duplex ultrasonography scanning as a reference method will permit the determination of the specificity, sensitivity, and accuracy of this approach.

In summary, it can be concluded that monitoring volume displacements induced by a change in leg position and recorded by C-PPG permits a noninvasive determination of venous outflow and inflow. The respective resistance changes can be also calculated using the changes in hydrostatic pressure. Statistically, highly significant outflow differences were observed between the normal control group and patients with DVT. Highly significant inflow differences were identified between the normal control group and patients with VVI. These findings

make C-PPG a fast and inexpensive physiologic technique to identify the presence or absence of these two types of venous disease.

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